University of North Carolina at Chapel Hill
Consent for Storing Biological Specimens With Identifying Information

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IRB Study # 07-1811
Consent Form Version Date: October 6, 2008

Title of Study: Pulmonary responses to exposure to low concentration ozone for 6.6 hours with moderate exercise in healthy young adults.

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What are some general things you should know about this research study?
Research studies are designed to gain scientific information that may help other people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies.

Research with blood, tissue and/or body fluids (specimens) can help researchers understand how the human body works. Research using specimens can also answer other questions. Many different kinds of studies use specimens. Some researchers may develop new tests to find diseases. Others may develop new ways to treat diseases. In the future, some research may help to develop new products, such as drugs.

You may refuse to allow us to have or store your specimen. If you are a patient with an illness, you do not have to be in the research study in order to receive treatment.

Details are discussed below. It is important that you understand this information so that you can make an informed choice. You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

The purpose of this study is to measure pulmonary function responses in healthy young adults during and immediately after exposure to low concentration ozone (0.0, 0.06 and 0.08 ppm) for 6.6 hours with moderate exercise and to examine 1) whether healthy young adults are affected by exposure to low ozone concentrations below the USEPA ozone standard, 0.08 ppm and 2) whether genetic variations play a role in individual's response to ozone exposure.

To study the effects of the ozone exposure we will examine for evidence of respiratory tract inflammation and markers of oxidative stress in lower airway sputum. We will collect blood samples from which presence or absence of specific antioxidant genes will be determined. This genotyping will help us to identify individuals who may be more susceptible to exposure to ozone and other oxidant pollutants.

All fluid samples will be labeled with a study subject number that does not include personal identification information and will be stored in a repository where only project members will have access to the samples. There is a need to store samples in such a repository because this will be an ongoing study where samples from subjects will be collected over an extended period of time. Storing of samples allows for all samples to be processed at the same time and also allows our scientist the opportunity to further study these samples with as yet unknown questions and techniques.

How will the specimen be collected?

Venipuncture

The medical station staff will draw approximately 20 ml of blood on the training day of study.

Lower airway sputum

You will be asked to inhale a mist of 3% salt water (saline) through a mouthpiece for 7 minutes while seated. Then you will be asked to rinse your mouths with tap water, gargle, clear your throat and blow your nose. You will then cough from deep in the chest and spit sputum into a sample cup. You will repeat this same procedure for 4% and 5% saline.

What will happen to the specimen?

Study samples will be stored in a secure room with restricted access at the U.S. Environmental Protection Agency Human Studies Facility located in Chapel Hill, North Carolina. The sample will be prepared, labeled with the study subject identification number, and stored indefinitely in a freezer for future testing. Names of subjects associated with ID numbers will be archived and locked; only medical and scientific personnel directly associated with this study will have access to this information. No personal identifying information will be attached to the biologic fluid samples. Portions of the samples may be shared with researchers at other scientific institutions, however, only coded samples will be sent. Under no circumstances will any identifying information be sent along with samples to outside investigators.

What are the possible benefits to you?

Benefits to you are unlikely. These studies (current and future) may provide additional information that will be helpful in understanding of whether exposure to low level ozone gas affects people. Ozone is one of a few pollutant gases identified by the U.S. Environmental Protection Agency and is present almost everywhere in the U.S. The results of this study may

ultimately play a role in regulation or standard setting for environmental exposure to ozone.

What are the possible risks or discomforts involved with being in this study?

This study might involve the following risks and/or discomforts to you:

1. Blood sampling will be performed by well-trained personnel, and entails only a risk of mild discomfort with the infrequent possibility of lightheadedness, fainting, infection or developing a bruise.
2. Breathing tests (plethysmography and spirometry): You may cough or become dizzy during these tests. You will be seated in a chair, and if these symptoms occur, they are usually only temporary.
3. Sputum induction may induce cough, throat irritation, or mild bronchoconstriction. These symptoms are generally transient. However, if a significant bronchoconstriction takes place (more than 20% drop in FEV_1), the procedure will be stopped and if necessary, 2 puffs of albuterol (bronchodilating drug) will be given.
4. The amount of moderate exercise you will be required to be performed during the exposure and testing procedures entails the potential, although minimal, risk of occasional muscle soreness, cramps or general fatigue. These discomforts are temporary and not harmful. Heart rate and rhythm will be monitored continuously. Exercise will be terminated at any time upon the request of the subjects.
5. The adhesive patches used as part of the heart monitoring system may cause some mild skin discomfort or discoloration.
6. Exposure to 0.08 ppm ozone has been studied at our institution and by other investigators and has shown minor effects in lung function in some individuals. You may experience some degree of airway irritation, cough, or tightness of chest with the exposure. These symptoms typically disappear 2 to 4 hours after exposure, but may last longer for particularly sensitive people. In the unlikely event that you develop medically significant symptoms, the exposure will be terminated and the appropriate medical intervention will be provided if required. Ozone also induces an inflammatory reaction that may last for 24 hours after exposure and may increase the chance of you catching a cold. Exposure to ozone at below 0.08 ppm ozone may not cause any significant effects in most of young healthy people.
7. There may be uncommon or previously unknown risks that might occur.

During all testing, a physician will be present or immediately available and can be present in the chamber or testing area within 1-2 min in response to an emergency. A group of physicians employed by EPA and UNC Center for Environmental Medicine, Asthma & Lung Biology have primary responsibility for medical coverage of studies conducted in the EPA Clinical Research Laboratory.

Risk of breach of confidentiality is minimal. You will be assigned a study number which will be used for data, not your name. The study number is all that will be entered into computer databases. All paper files which may contain your name or screening number are secure in the EPA building which has limited access 24 hours/day. A numeric coding system will be used to ensure that you cannot be directly identified from the samples alone.

Will there be any cost to you for storage of the specimens?
There will be no cost to you for the storage and use of the specimens for research purposes.

Will you receive anything for being in this study?
You will be receiving approximately $12.00 per hour for taking part in this study and additional fees for specific tests that will be performed on you during the study. You will receive a total of $1,339 if you complete the study with sputum induction procedure or a total of $1,285 if you complete the study without sputum induction procedure. In addition, if you travel from areas beyond Chapel Hill/Carrboro, you will be reimbursed for travel expenses commensurate with the US Government mileage rate in effect at the time. Parking will be provided or costs will be paid. Payments will be made after each segment of the study, unless the subject requests otherwise.

If you are unable to complete the study for voluntary reasons or failure to comply with eligibility requirements, you will receive full compensation for your participation up to that point in the study. If you are asked to stop participation by the investigators after enrollment in the study but prior to completion for involuntary reasons, you will be paid for the entire study, excluding completion bonus.

In the event a scheduled study activity must be cancelled by the investigators with less than 72 hours prior notice, you will be paid at the standard hourly rate ($12.00) for the time scheduled and canceled, and will be paid 50% of procedure fees up to a total maximum of $100 for canceled procedures. Cancellations could occur due to adverse weather conditions, equipment failure, or other unforeseen events. When feasible, you will be rescheduled.

The following table details the expected compensation for completion of the entire study:

Pre-study qualifications	
recruitment screening	$15
physical exam	$15
	Pre-study qualification total = $30
Training day/Day 1 (3 hours)	
venipuncture (~20ml, gene analysis)	$30
sputum induction	$30
time (3h @$12/h)	$36
	Day 1 total = $96
Exposure day/Day 2 (8 hours)	
on time arrival bonus	$25
chamber exposure (6.6 hours@$24/hr)	$159
spirometry (5@$20)	$100
plethysmography (2@$20)	$40
time (2h @$12/h)	$24
lunch:	$5
	Day 2 total for completion of exposure = $353
Exposure day/Day 3 (8 hours)	
Same as Day 2	Day 3 total for completion of exposure = $353

Exposure day/Day 4 (8 hours)
Same as Day 2 — Day 4 total for completion of exposure = $353

Follow-up day: Day 5 (2 hours)*
time (2 hr@$12/hr) — $24
sputum induction — $30
Day 5 for sputum induction = $54*

Protocol Completion Bonus — $100

TOTAL for completion of three exposures and sputum induction = $1339
TOTAL for completion of three exposures but no sputum induction = $1285

* Follow-up day sputum induction will be performed in the morning immediately following one of the three exposure days in those qualified for sputum induction on Day 1 (training day).

Money received by participants in research studies is normally treated as ordinary income by taxing authorities and we will report payments made to you to the Internal Revenue Service as required by law. The money is not intended to coerce completion or participation, but to emphasize the importance of all the visits, and to signify the importance of your time and commitment to the research study.

Who owns the specimens?

Any blood, body fluids, or tissue specimens obtained for the purpose of this study become the exclusive property of the U.S. Environmental Protection Agency. The researchers may retain, preserve or dispose of these specimens and may use these specimens for research that may result in commercial applications. There are no plans to compensate you for any future commercial use of these specimens.

How will your privacy be protected?

You will be assigned a study identification number. Names of subjects associated with ID numbers will be archived and locked; only medical and scientific personnel associated with this study will have access to this information. No personal identifying information will be attached and/or recorded in the data log sheets, biologic samples, or electronic data sets. No subjects will be identified in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, the U.S. Environmental Protection Agency and UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies for purposes such as quality control or safety.

Study samples will be stored in a secure room with restricted access. The sample will be prepared and stored indefinitely in a freezer for future testing. Portions of the samples may be shared with researchers at other scientific institutions, however, only coded samples will be sent. Under no circumstances will any identifying information be sent along with samples to outside investigators. All medical records generated during this study will be kept in the medical records office at the EPA Human Studies Facility. The Medical Station is locked when not attended by

study staff, and the EPA Human Studies Facility has limited access to authorized individuals only, 24 hours/day for 7 days/week.

Will researchers seek approval from you to do future studies involving the specimens?

By signing this consent form, you are giving your permission for researchers to use your specimens as described above. Current and future research is overseen by a committee called the Institutional Review Board (IRB). The role of the IRB is to protect the rights and welfare of research participants.

In some cases, the IRB may require that you be re-contacted and asked for your consent to use your specimens in a specific research study. You have the right, at that future time, not to participate in any research study for which your consent is sought. Refusal to participate will not affect your medical care or result in loss of benefits to which you are entitled.

Will you receive study results of future research involving your specimens?

Most research with your specimens is not expected to yield new information that would be meaningful to share with you individually. In rare cases, you may be offered the opportunity to receive information about the results of research in which the specimens were used (for example, findings that would affect your medical care).

Can you withdraw the specimens from the research study?

If you decide that you no longer wish for the specimens to be stored, you should contact the researchers on the front page of this form. You may also contact the Institutional Review Board, University of North Carolina at Chapel Hill, 919-966-3113, Medical School Building 52, CB 7097, Chapel Hill, NC 27599, or by email at IRB_subjects@unc.edu. It is best to make your request in writing.

Any analysis in progress at the time of your request or already performed prior to your request being received by the researcher will continue to be used as part of the research study. Once the researchers have been notified, your specimens would be destroyed. If you do not make such a request, the specimens may be stored forever. The researchers may choose to destroy the specimens at any time.

What will happen if you are injured by this research?

All forms of human health research involve some risk of injury or illness. Despite our high level of precaution, you may develop an injury or illness due to participating in this study. If you develop an injury or illness determined by an appointed USEPA physician to be due to your participation in this research, the EPA will reimburse your medical expenses to treat the injury or illness up to $5000. If you believe your injury or illness was due to a lack of reasonable care or other negligent action, you have the right to pursue legal remedy. The Federal Tort Claims Act, 28 U.S.C. S 2671 et seq., provides for money damages against the United States when personal injury or property loss results from the negligent or wrongful act or omission of any employee of the EPA while acting within the scope of his or her employment. Signing this consent form does not waive any of your legal rights or release the investigator, the sponsor, the institution, or its agents from liability for negligence. If a research-related injury occurs, you should contact the Director of the EPA NHEERL Human Research Protocol Office at 919-966-6217.

Who is sponsoring this study?
This research is funded by the United States Environmental Protection Agency. Several of the investigators including the Principal Investigator are federal employees. The researchers do not, however, have a direct financial interest in the final results of the study.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have questions, you should contact the researchers listed on the first page of this form.

What if you have questions about your rights as a research subject?
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject you may contact, anonymously, if you wish, the Institutional Review Board at 919-966-3113 or by email to IRB_ subjects@unc.edu. You may also contact the Director of the EPA NHEERL Human Research Protocol Office at 919-966-6217.

Subject's Agreement:
I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate. I agree to my specimen(s) being stored with the identifying code(s).

_____ _____
Signature of Research Subject Date

_____
Printed Name of Research Subject

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent